Case Report

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Double Positive Anti-GBM and ANCA Along with Hyponatremia: Case Report

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ABSTRACT

On rare occasions, patients with Goodpasture's syndrome (GPS) present with both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA). Concurrent ANCA and anti-GBM disease is rare with a high mortality rate. Here we present a case of both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA) complicated with hyponatremia.

Keywords: Goodpasture's Syndrome (GPS); Anti-Glomerular Basement Membrane (GBM); Antineutrophil Cytoplasmic Antibody (ANCA); Hyponatremia

Abbreviations: GPS: Goodpasture's Syndrome; GBM: Anti-Glomerular Basement Membrane; ANCA: Antineutrophil Cytoplasmic Antibody; CGN: Crescentic Glomerulonephritis; CRRT: Continuous Renal Replacement Therapy; ELISA: Enzyme-Linked Immunosorbent Assay

Introduction

On rare occasions, patients with Goodpasture's syndrome (GPS) present with both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA) [1]. Rutgers, et al. [2] reviewed Limburg renal biopsy registry (1978 -2003) included 1373 cases of crescentic glomerulonephritis (CGN) and reported 10 double-positive cases. Concurrent ANCA and anti-GBM disease is rare with high mortality rate. Aggressive immunosuppression with steroids, cyclophosphamide and plasma exchange can induce remission and preserve renal function. However, long-term monitoring for relapses should occur [1]. Here we present a case of both anti-glomerular basement membrane (GBM) and antineutrophil cytoplasmic antibody (ANCA) complicated with hyponatremia.

Case Presentation

62-year-old Caucasian female with past medical history significant for hypothyroidism, recurrent nasal allergies admitted with abdominal pain and distention. Presenting to the emergency department with a complaint of generalized abdominal pain for 3 days prior to presentation for which she saw her physician who prescribed magnesium citrate resulting in loose stool with 3-4 small bowel movements associated with nausea and vomiting. She endorsed having burning at the end of urination for 2 days. She also noticed pinkish color urine for three to four weeks prior to presentation. Also, of note is taking 400 mg Motrin once to twice a day for the previous 3 to 4 weeks. Remainder of the review of system was unremarkable. On presentation her blood pressure 151/88 mmHg, pulse 74 bpm, Temp 98.6 F, Resp 15 br/m, spO2 94% on room air, BMI 23.52. Physical examination revealed an anxious appearing female with normal appearance. Chest and cardiac exam were initially unremarkable without any abnormal sounds. Soft, mild tenderness, and slight distention noticed on abdominal examination. Initial basic work-up revealed hemoglobin of 7.8 g/dL, WBC 15.3, BUN 116 mg/dL, serum creatinine 12.4 mg/dL, serum sodium 111 mEq/L potassium of 5.3 mEq/L.

Urine analysis dipstick positive for protein and blood, microscopy shows RBCs >100 hpf. CT scan abdomen with IV contrast demonstrated diffuse mesenteric infiltration, moderate amount of free fluid within the pelvis and right-sided pleural effusion with infiltration. Remaining oliguric from admission she developed shortness of breath treated with furosemide 80 mg without response. The initial differential diagnosis included volume depletion, NSAID induced nephropathy and vasculitis. Her respiratory status worsened requiring high flow oxygen and chest x-ray demonstrating the classic batwing pattern of pulmonary hemorrhage and CT scan demonstrated segmental and lobar distribution infiltrates involving predominantly the upper lobes (Figures 1 & 2). Bronchoscopy demonstrated bloody secretion consistent with pulmonary hemorrhages. In the setting of hematuria and proteinuria a serological work-up revealed a low C3 of 83, C4 18.8, ANA and dsDNA negative, positive for ANCA titers 1: 640 with MPO 72 and anti-GBM of 106. Hemoglobin dropped to 6.3 transfused with 2 unit of packed RBCs with furosemide. Oliguria persisted developing volume overload with worsening hypoxia and hyponatremia resulting in transfer to critical care unit and initiation of continuous renal replacement therapy (CRRT).

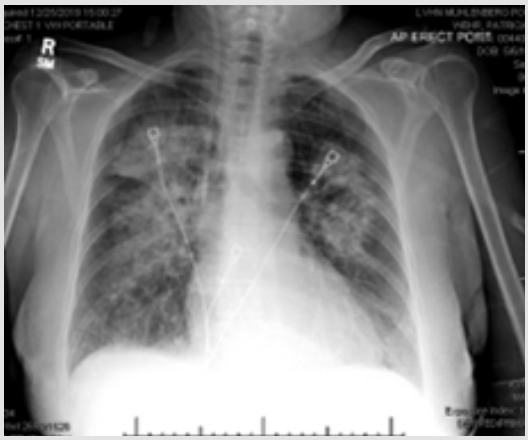

Figure 1: Chest X-Ray demonstrating classic batwing pattern of pulmonary hemhorrage.

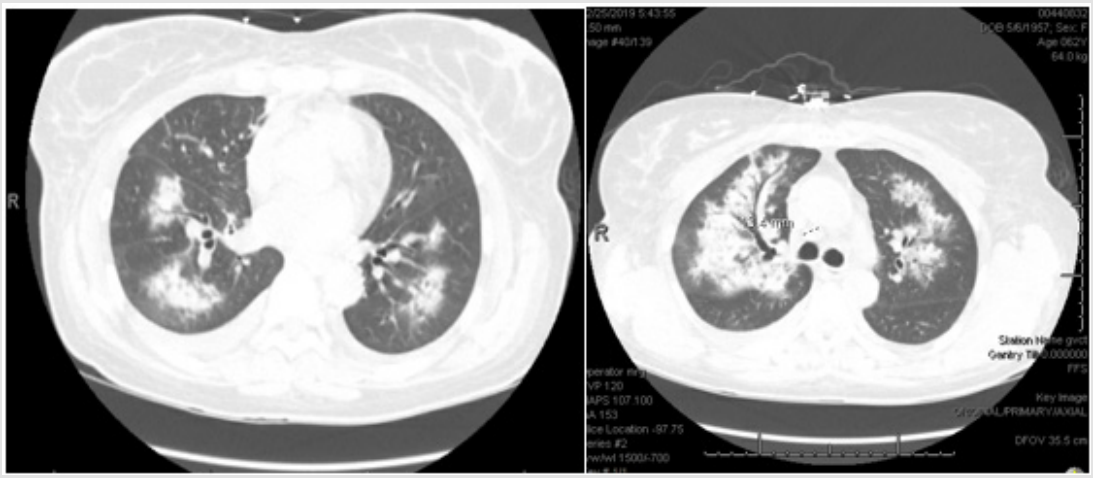

Figure 2: CT scan of chest demonstrating the segmental and lobar distribution infiltrates involving predominantly the upper lobes.

Given the pulmonary hemorrhage, hematuria, and acute kidney failure methylprednisolone 500 mg intravenously daily for 3 doses was initiated due to concern for Good Pasture syndrome including plans for plasmapheresis and kidney biopsy. Hyponatremia, with a sodium of 111, was corrected at 6 to 8 mEq/L in 24 hours with support of CRRT low dialysate flow and IV D5W. She was started on plasmapheresis and IV Cyclophosphamide 500 mg prior to renal biopsy. Persistent anemia with a hemoglobin dropping to 6.2 resulted in packed RBC transfusion. Kidney biopsy demonstrated a diffuse necrotizing and crescentic glomerulonephritis consistent with anti-GBM disease associated with MPO-ANCA. (Figure 1) Immunofluorescence findings of linear staining of the glomerular basement membrane of 2-3+ intensity for IgG with 1-2+ kappa and lambda support the diagnosis of anti-GBM disease. CRRT transitioned to intermittent hemodialysis, and plasmapheresis was continued 3 times in a week until GBM titers 0, completing a course of Cyclophosphamide 500 every 2 weeks for 6 doses. After 12 session of plasmapheresis anti-GBM titer trended down to 18 and she was maintained on oral prednisone for 6 months. (Figure Unfortunately, she remained dialysis dependent and is now listed for a kidney transplant. There has been no recurrence of pulmonary hemorrhage in the past 3 years (Figures 3 & 4).

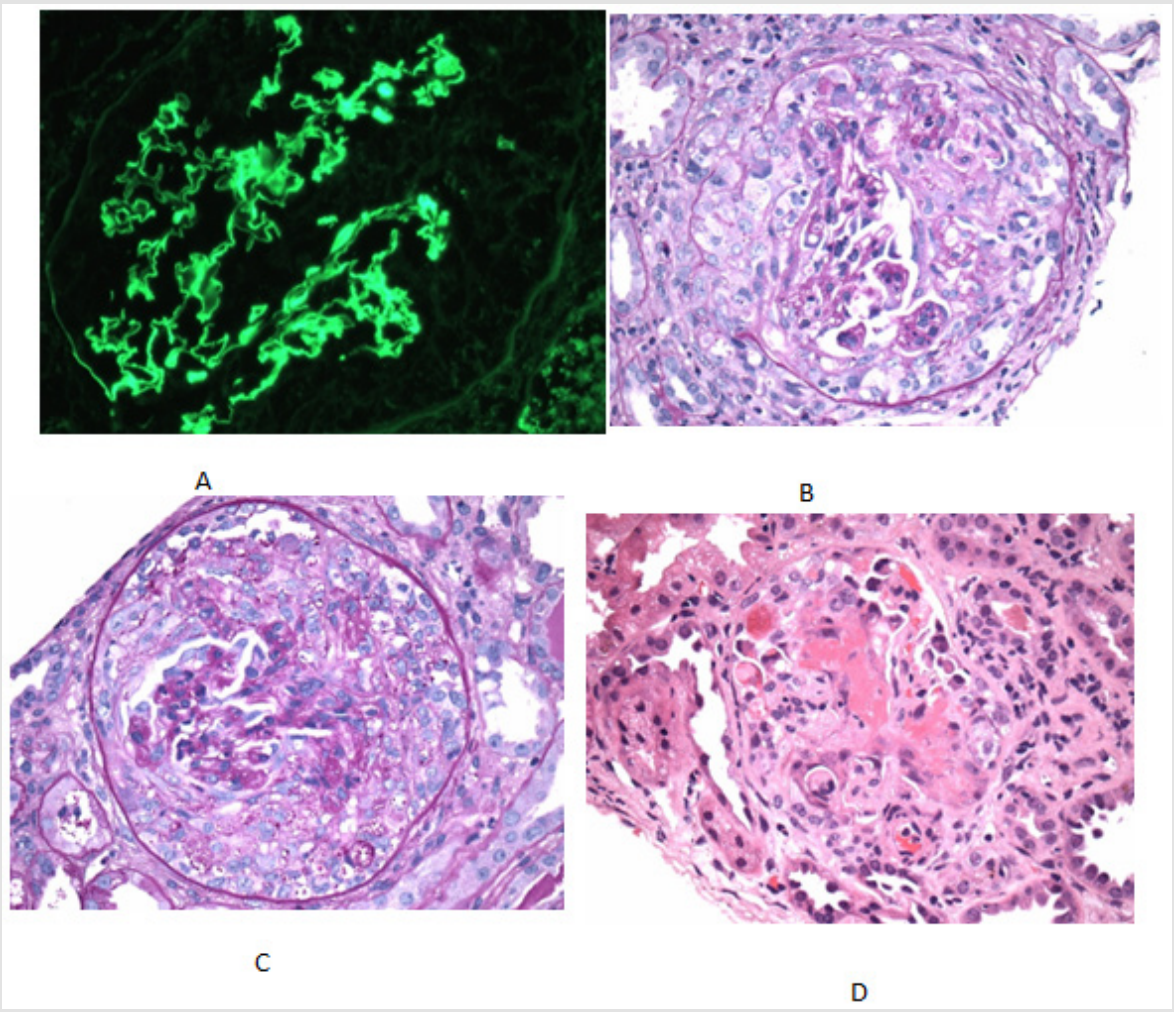

Figure 3: Kidney biopsy demonstrated a diffuse necrotizing and crescentic glomerulonephritis consistent with anti-GBM disease associated with MPO-ANCA. (A) Immunofluorescence findings of linear staining of the glomerular basement membrane of 2-3+ intensity for IgG with 1-2+ kappa and lambda support the diagnosis of anti-GBM disease (B, C and E) demonstrate the cellular crescents in this rapidly progressive diffuse necrotizing glomerulonephritis.

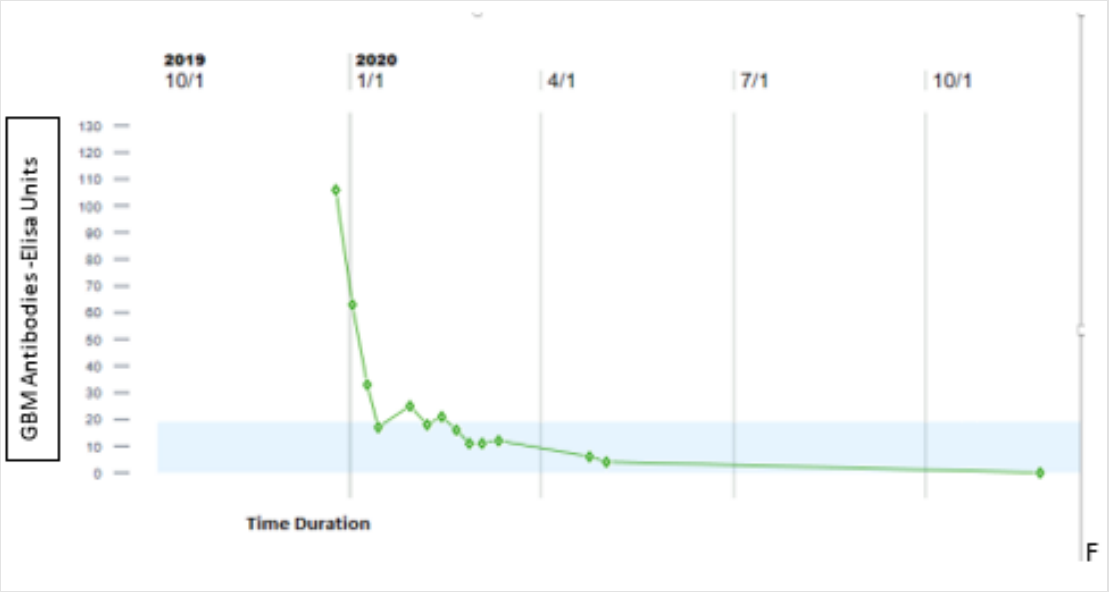

Figure 4: Graph represents levels of anti-GBM antibodies measured by the enzyme-linked immunosorbent assay (ELISA) and expressed in arbitrary ELISA units as indicated by the right vertical axis after initiation of therapy with plasmapheresis, steroids and cyclophosphamide.

Discussion

Good Pasture syndrome is a rare life-threatening autoimmune vasculitis characterized by diffuse alveolar hemorrhages, Crescentic glomerulonephritis, and severe metabolic derangements. The incidence of this diseases is rare with a prevalence in a European population of 1 to 2/million/year 3. We present the case of double anti GBM and ANCA positive titers causing pulmonary and renal manifestation. The basic mechanism of anti-GBM disease is formation of type IV collagen alpha-3 chain in alveolar and glomerular basement membrane [3,4]. Antineutrophil cytoplasmic antibody trigger inflammatory cascade by the activation of excessive neutrophils [5]. Antiglomerular basement membrane antibodies and ANCA antibodies can be coexist in 20 to 50% of patients known as double positive disease [6]. Clinically with double positive titers have poor renal outcome along with extrarenal manifestation. Hallmark of anti-GBM and ANCA vasculitis is crescents formation due to inflammation and multilayer proliferating cells in Bowman space seen in renal biopsy [7]. These patients have been treated aggressively with plasmapheresis cyclophosphamide and steroid to reduce antibody burden and damage.

Observational study shows patients with positive anti-GBM titers survival rate improved after plasmapheresis compared with immunosuppressive alone [8]. Majority of patient with severe pulmonary hemorrhage responds with combination of plasmapheresis and immunosuppressive which was seen in a case series where 90% of patients recovered completely [9]. Studies have demonstrated that patients who require immediate renal replacement therapy have poor renal outcome. Our patient required hemodialysis on the second hospital day and despite rapid aggressive therapy with pulse solumedrol, plasmapheresis, and cyclophosphamide never recovered kidney function. Interestingly, she presented with severe hyponatremia of sodium 111 mEq/L which was managed with continuous renal replacement therapy and hypotonic IV infusion to limit sodium correction to an acceptable rate. In rare cases patient presents with severe hyponatremia due to SIADH in the setting of vasculitis which has been reported [10]. As mentioned, double positive titers should be treated aggressively with plasmapheresis and immunosuppression due to the severe renal and pulmonary manifestation seen. However, patients with ANCA associated vasculitis have undetectable anti-GBM antibodies in 5% of cases [11]. Plasmapheresis should be considered in the treatment regimen when diffuse pulmonary hemorrhage is present with the understanding that it also can be associated with an increase incidence of hemorrhage [12,13].

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